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Date: March 1, 2004 By: Carol A. See

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PATENT
Docket No. GC723

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
Bott et al.	)	Group Art Unit: 1645
	)	
Serial No.: 10/092,227	)	Examiner: K. Kerr
	)	
Filed: March 5, 2002	)	
	)	
For: High Throughput Mutagenesis Screening Method	)	

RESPONSE TO RESTRICTION REQUIREMENT MAILED JANUARY 29, 2004

Commissioner for Patents
U.S. Patent and Trademark Office
Arlington, VA 22202

Sir:

In response to the Restriction Requirement mailed January 29,2004, Applicant respectfully requests that the following amendments be made. A complete list of the Claims, including marked-up versions of the rewritten, added, withdrawn, and/or cancelled claims is provided below, beginning on page 2. None of the amendments to the Claims is intended to narrow the scope of any of the amended Claims within the meaning of *Festo*[1]. The Remarks begin on page 6.

[1] *Festo Corp. v. Shoketsu Kogyo Kabushiki Co.*, No. 95-1066, 2000 WL 1753646 (Fed. Cir. Nov. 29, 2000).

LIST OF CLAIMS, SHOWING THE STATUS OF EACH CLAIM

1. (Original) A method for obtaining a variant having one or more desired protein properties comprising: selecting amino acid sites in a protein for mutation; performing mutagenesis at the selected mutation sites to create a library; screening the library for variants having one or more desired protein properties; grading the mutation sites of the variants for the one or more desired protein properties; selecting one or more variants having a desirable grade as a template for, with feedback from the grading, creating and screening additional libraries, whereby the method utilizes cooperative mutations to obtained a variant having at least two mutations.

2. (Original) The method of claim 1 wherein said mutagenesis is performed by site-saturation mutagenesis and wherein selecting amino acid sites is performed by utilizing protein structural considerations.

3. (Original) The method of claim 2 wherein creating and screening additional libraries is performed by repeating site-saturation mutagenesis at mutation sites having desirable grades and performing site-saturation mutagenesis at new sites on new libraries.

4. (Original) The method of claim 3 wherein performing site-saturation at new sites is performed by selecting sites located near mutation sites having desirable grades.

5. (Original) The method of claim 2 wherein the protein structural considerations are binding site location, three-dimensional

structure, amino acid sequence, nature of chemical reaction, or nature of chemical binding.

6. (Original) The method of claim 1 wherein the protein property is an enzyme property.

7. (Original) The method of claim 6 wherein the enzyme property is one or more of catalysis, binding, or stability.

8. (Original) The method of claim 1 wherein the screening for one or more variants is performed by selecting and conducting appropriate assays for the one or more protein properties of interest.

9. (Original) The method of claim 1 wherein grading is performed by identifying trends.

10. (Original) The method of claim 9 wherein identifying trends is performed by plotting a spatial distribution of graded sites on a three-dimensional rendition of the protein.

11. (Original) The method of claim 9 wherein identifying trends is performed by plotting amino acid mutation identities.

12. (Original) The method of claim 9 wherein identifying trends is performed by plotting a distribution of graded mutation sites.

13. (Original) The method of claim 2 wherein creating and screening additional libraries is performed by screening the additional libraries for the desired protein properties and repeating site-saturation mutagenesis until a desired protein property goal is attained.

14. (Original) A method for obtaining a variant enzyme having one or more desired properties comprising: selecting amino acid sites utilizing a three-dimensional rendition of the enzyme; performing site-saturation mutagenesis at the selected mutation sites to create a library; screening the library for variants having one or more desired properties; grading the mutation sites of the variants for the one or more desired properties; selecting one or more variants having a desirable grade as a template; using the template and feedback to repeat site-saturation mutagenesis at mutation sites having desirable grades and to perform site-saturation mutagenesis on new libraries at new sites.

15. (Original) The method of claim 14 wherein the one or more desired properties are substrate activity, thermostability , stability relative to reaction environment, ionic strength range of stability, pressure stability, or pH range of stability.

16. (Original) The method of claim 14 wherein the one or more desired properties is substrate activity and thermostability.

17. (Original) The method of claim 14 wherein the enzyme is cutinase.

18. (Original) A process for the production of a cutinase variant with hydrolytic activity on polyester, the cutinase from Pseudomonas species, the process comprising: utilizing a three-dimensional model to select for mutation amino acid sites likely to demonstrate hydrolytic activity; performing site-saturation mutagenensis at the selected mutation sites on a library; screening the library for variants using assays to detect polyesterase activity and thermostability; grading the mutated sites as beneficial, neutral or

detrimental for both polyesterase activity and thermostability; selecting a variant having at least one beneficial grade; creating new and repeat libraries using the selected variant and feedback from the grading.

REMARKS

The present application was originally filed with 18 Claims. In the present Restriction Requirement, the Examiner has restricted the Claims into two species, namely:

a) Methods of obtaining variants using crystal structures; and

b) Methods of obtaining variants not using crystal structures.

The Examiner argues that the Groups represent separate and patentably distinct species. While Applicants must respectfully traverse the restriction requirement, Applicants hereby elect the species in Group a), directed towards methods of obtaining variants using crystal structures. Applicants understand that Claims 14-18 will be examined first, but if no prior art is found, all of the Claims will be examined in the first Office Action. As it is possible for all Claims to be examined in the present application, Applicant has not withdrawn nor cancelled any Claims. Should the Examiner have any questions regarding this application, she is encouraged to call the undersigned.

Respectfully submitted,

Date: March 1, 2004

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